REMARKS

Claims 1-3, 5-8, 11, 12, 15, 16 and 84-94 are currently under examination following entry of the foregoing Amendment. Claims 4, 13 and 14 are canceled; Claims 1, 16 and 84 are amended; and new Claims 85-94 added. The claim amendments and issues raised in the outstanding Office Action will be addressed individually below.

Claim Amendments.

Claim 1 has been amended to incorporate the recitations of Claims 4 and 13. Accordingly, Claims 4 and 13 have been canceled.

Claim 16 has been amended to recite that the vector is an alphavirus vector. This claim amendment is supported throughout the application.

Claim 84 has been amended to incorporate the recitations of Claim 13.

New dependent Claims 85, 86 and 88–93 depend from Claim 84 and are analogous to pending dependent Claims 2, 3, 5-8, and 13-15. These claims are added to provide a more complete claim set.

New Claim 87 recites that the Venezuelan Equine Encephalitis Virus particles are replicon particles. This recitation is supported throughout the application.

New independent Claim 94 is a re-writing of Claim 1 to incorporate the recitations of dependent Claim 14. Accordingly, Claim 14 has been canceled.

Information Disclosure Statement.

The Examiner has indicated on page 2, paragraph 3, that reference #1 (Vaccines Pushing Beyond Polio, Forbes ASAP, May 31, 1999) in the Information Disclosure Statement submitted on August 18, 1999 has not been considered because the submitted copy was incomplete. Applicants will submit a better copy of this reference shortly.

Claim Objections.

Claims 1 and 84 stand objected to, the Examiner stating that the adjective "immunogenic" should be amended to "immunogenically." Claims 1 and 84 have been amended as suggested; accordingly, Applicants respectfully request that the outstanding claim objections have been overcome and should be withdrawn.

Rejections under § 112, second paragraph.

Claims 1-8, 11-15 and 84 stand rejected under 35 U.S.C. § 112, second paragraph on several grounds of indefiniteness. The individual rejections will be addressed below. Claims 4, 13 and 14 have been canceled. This rejection will be addressed with respect to pending Claims 1-3, 5-8, 11, 12, 15, and 84-94.

Claims 1 and 84 stand rejected for indefiniteness for reciting a "composition comprising infectious alphavirus particles in an immunogenically effective amount, wherein said alphavirus particles comprise one or more heterologous nucleotide sequences encoding an antigen" (emphasis added). The Office Action states that "the claims have been interpreted as drawn to a composition consisting essentially of alphavirus particles comprising a heterologous nucleotide sequence."

Applicants submit that the recitation of "a composition comprising infectious alphavirus particles" is standard claim language and does not render the claims indefinite. For example, the composition may contain other therapeutic or immunogenic agents. Moreover, Applicants respectfully point out that the Patent Office has previously issued patents that use this claim language, *see e.g.*, Claim 1 of U.S. Patent No. 6,156,558 (copy enclosed).

In view of the foregoing, Applicants submit that Claims 1 and 84 are not indefinite and respectfully request that the rejection on this basis be withdrawn.

Claim 6 stands rejected as indefinite, the Office Action stating that "[a]bsent a teaching of the reference sequence which is the basis for the attenuating mutations, the claims are indefinite. New Claim 88 also recites the

attenuating mutations of Claim 6. The recited attenuating mutations are disclosed in U.S. Patent Nos. 5,643,576; 5,505,947; and 5,185,440 (copies enclosed herewith). These patents are incorporated by reference in the present application at page 19, lines 25-29. Accordingly, Applicants submit that Claims 6 and 88 are definite, and respectfully request that the outstanding rejection against Claim 6 be withdrawn.

Claim 13 stands rejected as indefinite for reciting an improper Markush group. Claim 13 has been canceled, and Claim 1 has been amended to incorporate the recitations of Claim 13 with modifications to more particularly point out the features of the claimed invention. Claim 1 has been amended to recite "an artificial cancer antigen that is not normally expressed by a cancer cell, wherein said artificial cancer antigen is selected from the group consisting of a helper T cell epitope, a cytotoxic T cell epitope, a T-dependent B cell epitope, and a T-independent B cell epitope." New Claim 91 contains a similar recitation. Applicants submit that Claims 1 and 91 particularly point out and distinctly claim the subject matter of the invention, thereby overcoming the outstanding rejection.

Claim 13 further stands rejected for recitation of particular classes of T- and B-cell epitopes. Claim 13 has been canceled, and Claim 1 has been amended to incorporate the recitations of Claim 13 as described in the previous paragraph. Applicants submit that the meanings of the recited terms would be sufficiently clear to those skilled in the art. For example, a "helper T cell epitope" is an epitope that elicits a strong helper T cell response. Accordingly, Applicants respectfully request that the outstanding indefiniteness rejection be withdrawn.

The Claims are Novel over Song et al.

Claims 1-3, 11-15 and 84 stand rejected under 35 U.S.C. § 102 (a) as anticipated by WO 97/24447 (Song et al.). Claims 13 and 14 have been canceled. This rejection will be discussed below with respect to pending Claims 1-3, 11, 12, 15, and 84-94.

Applicants respectfully disagree with this rejection. Nonetheless, to expedite the prosecution of this application, the independent claims have been amended herein to incorporate the recitations of Claim 4 ("wherein said alphavirus particles comprise one or more attenuating mutations"), without acquiescing to the outstanding rejection. As Claim 4 is free of the present rejection, Applicants submit that Claims 1-3, 11, 12, 15, and 84-94 by incorporating the recitations of Claim 4 are also free of this rejection, and respectfully request withdrawal thereof.

The Claims are Novel over Dubensky et al.

Claims 1-3, 7, 11-15, and 84 stand rejected under 35 U.S.C. § 102 (b) over WO 95/07994 (Dubensky et al.). Claims 13 and 14 have been canceled. Accordingly, this rejection will be addressed with respect to pending Claims 1-3, 7, 11, 12, 15, and 84-94.

Applicants respectfully disagree with the rejection over Dubensky et al. However, to expedite the prosecution of this application, the independent claims have been amended herein to incorporate the recitations of Claim 4 ("wherein said alphavirus particles comprise one or more attenuating mutations"), without acquiescing to the outstanding rejection. As Claim 4 is free of the present rejection, Applicants submit that Claims 1-3, 7, 11, 12, 15, and 84-94 by incorporating the recitations of Claim 4 are also free of this rejection, and respectfully request withdrawal thereof.

The Claims are Novel over Johnston et al.

Claims 1-8, 11-13 and 15 stand rejected under 35 U.S.C. § 102 (b) over WO 95/32733 (Johnston et al.). Claims 4 and 13 have been canceled. Accordingly, this rejection will be addressed with respect to pending Claims 1-3, 5-8, 11, 12 and 94.

While Applicants respectfully disagree with the present rejection, the claims have been amended to expedite the prosecution of this application, without acquiescence to this rejection.

Claim 94 is essentially a rewriting of Claim 1 to incorporate the recitations of Claim 14. As Claim 14 is free of the present rejection, Applicants submit that Claim 84 is also free of this rejection.

Claim 1 has been amended to essentially incorporate the recitations of Claim 13. Applicants submit that canceled Claim 13 was not properly subject to the rejection over Johnston et al. Claim 1, as amended, recites "an artificial cancer antigen that is not normally expressed by a cancer cell, wherein said artificial cancer antigen is selected from the group consisting of a helper T cell epitope, a cytotoxic T cell epitope, a T-dependent B cell epitope, and a T-independent B cell epitope." Applicants submit that Johnston et al. neither discloses nor suggests the recited epitopes or an alphavirus vector expressing the same. Johnston et al. describes VEE vectors expressing an immunogen, but not specifically a helper T cell epitope, a cytotoxic T cell epitope, a T-dependent B cell epitope, or a T-independent B cell epitope, as recited by Claim 1.

Accordingly, Applicants submit that the subject matter of amended Claim 1 is both novel and unobvious over Johnston et al. Likewise, Applicants submit that the subject matter of dependent Claims 2, 3, 5-8, 11, 12 and 15 is novel and unobvious over Johnston et al. Accordingly, Applicants respectfully request that the outstanding rejection over this reference be withdrawn.

The Claims are Patentable over Johnston et al. in view of Falo et al.

Claims 1-8, 11-16 and 84 stand rejected under 35 U.S.C. § 103 (a) as unpatentable for obviousness over Johnston et al. in view of 5,951,875 (Falo et al.). Claims 4, 13 and 14 have been canceled. This rejection is addressed below with respect to pending Claims 1-3, 5-8, 11, 12, 15, 16 and 84-94.

Johnston et al. teaches methods of producing an immune response by administration of a live Venezuelan Equine Encephalitis (VEE) virus expressing a heterologous immunogen. Falo et al. teaches a method of cross-priming a mammalian subject with an artificial tumor antigen,

specifically, ovalbumin conjugated to iron beads. Falo et al. teaches that the artificial tumor antigen may be delivered by "(1) particulate antigen delivery; (2) peptide pulsing; or, (3) polynucleotide delivery" (Falo et al., Col. 4, lines 59-62).

In contrast with the present application, neither Johnston et al. nor Falo et al. teaches methods of using an alphavirus vector to deliver an artificial cancer antigen for prophylactic or therapeutic treatment of cancer or tumors. The claimed vectors and methods are neither disclosed nor suggested by the cited references, taken alone or in combination. Furthermore, one of ordinary skill in the art at the time of invention would have had no reasonable expectation of success in achieving the present invention, which reasonable expectation is required to maintain the current obviousness rejection. *In re Dow Chemical*, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988).

The present inventors have found that alphavirus vectors are effective in providing protection against tumor establishment and in causing regression of established tumors (specification, Examples 4-6). These unexpected and advantageous properties of alphavirus vectors for cancer immunotherapy are neither disclosed nor suggested by Johnston et al. nor Falo et al., alone or in combination Accordingly, respectfully submit that the presently-claimed invention of Claims 1-3, 5, 6-8, 11, 12, 15, 16, and 84-94 is novel and unobvious over Johnston et al. in view of Falo et al.

With particular respect to Claim 1, this Claim has been amended to incorporate the recitations of Claim 13. As described in the previous section, Johnston et al. does not describes alphavirus vectors expressing a helper T cell epitope, a cytotoxic T cell epitope, a T-dependent B cell epitope, or a T-independent B cell epitope, as recited by Claim 1. Likewise, Falo et al. fails to disclose an artificial cancer antigen, wherein the artificial cancer antigen is specifically one of the recited T- or B-cell epitopes. Accordingly, Applicants submit that the subject matter of independent Claim 1 (and dependent Claims 2, 3, 5-8, 11, 12, 15) is unobvious over Johnston et al. in view of Falo et al.

With respect to new Claim 94, this claim is essentially a rewriting of Claim 1 to incorporate the recitations of Claim 14 ("wherein said artificial cancer antigen is a cell-surface protein or peptide"). Neither Johnston et al. nor Falo et al. disclose or suggest the desirability of using a cell-surface protein or peptide as an artificial cancer antigen. Accordingly, Applicants submit that the subject matter of new Claim 94 is free of the outstanding obviousness rejection.

In view of the foregoing discussion, Applicants submit that Claims 1-3, 5-8, 11, 12, 15, 16, and 84-94 are patentable over Johnston et al. in view of Falo et al., and request that the rejection on that basis be withdrawn.

Conclusion.

The points and concerns raised in the Office Action having been addressed in full, it is submitted that this application is in condition for allowance, which action is respectfully submitted. Should the Examiner have any remaining concerns, it is requested that the Examiner contact the undersigned representative to expedite the prosecution of this application.

Respectfully submitted,

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Enclosure: U.S. 6,156,558
U.S. 5,643,576
U.S. 5,505,947
U.S. 5,185,440

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CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to Commissioner for Patents, Washington, DC 20231, on February 20, 2001.

Marjorie J. Pfeiffer
Date of Signature: February 20, 2001